EXHIBIT H

DOI: 10.1111/j.1471-0528.2011.03082.x
www.bjog.org

Primary surgical repair of anterior vaginal prolapse: a randomised trial comparing anatomical and functional outcome between anterior colporrhaphy and trocar-guided transobturator anterior mesh

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Accepted 25 May 2011. Published Online 22 August 2011.

Objective To compare anterior colporrhaphy with a trocar-guided transobturator mesh procedure (Avaulta® anterior).

Design Randomised, controlled trial.

Setting Three teaching hospitals.

Population Women with a symptomatic cystocele at least stage II requiring primary surgical correction.

Methods A total of 125 women were assessed at baseline and 1-year follow up. A sacrospinous hysteropexy or posterior colporrhaphy was performed when indicated.

Main outcome measures The primary outcome was the difference in anatomical cure (defined as Pelvic Organ Prolapse-Quantification <stage II cystocele). Secondary outcomes were complications, self-reported urogenital symptom severity, and quality of life, as measured with validated questionnaires.

Results In all, 64 women were allocated to the anterior colporrhaphy group and 61 to the mesh group; 58/64 women versus 56/61 completed 12 months of follow-up analysis. Compared with the anterior colporrhaphy group, the mesh reduced the risk of anatomical failure at 12 months follow up from 59 to 9% (risk reduction 50.3%, 95% CI 35.5–65.1). Only three (5%) re-operations for anatomical failure in the anterior colporrhaphy group were performed versus 0% in the mesh group. Functional outcome improved significantly at 12 months on almost all domains, with similar results between groups. Mesh exposure occurred in two (4%) women. Baseline dyspareunia disappeared significantly more often after an anterior colporrhaphy (80%) than in the mesh group (20%). There was a trend towards more *de novo* dyspareunia in the mesh group (15% versus 9%).

Conclusions Primary cystocele repair with trocar-guided transobturator mesh resulted in a statistically significant better anatomical outcome compared with the anterior colporrhaphy. However, functional outcome was similar between groups.

Keywords Anterior colporrhaphy, cystocele, transobturator mesh.

Please cite this paper as: Vollebregt A, Fischer K, Gietelink D, van der Vaart C. Primary surgical repair of anterior vaginal prolapse: a randomised trial comparing anatomical and functional outcome between anterior colporrhaphy and trocar-guided transobturator anterior mesh. BJOG 2011;118:1518–1527.

Introduction

Surgery is the treatment of choice for women with symptomatic cystocele if conservative treatments like pelvic floor muscle exercises and vaginal pessary therapy have failed. An anterior colporrhaphy, in which the woman's native tissue is used in the repair, has been the standard technique.[1,2] However, with this technique, recurrences are reported in 20–70% of women.[3–7]

In recent years, the use of synthetic mesh to prevent cystocele recurrences has become increasingly popular. Initially, the synthetic mesh was interpositioned between the bladder and vaginal mucosa; however, more recently, trocar-guided transobturator synthetic mesh kits became commercially available. At the time this trial was designed, in 2007, no randomised studies had been published comparing anterior colporrhaphy with the trocar-guided transobturator mesh procedure. Observational studies showed

the use of mesh to be anatomically effective; however, there were concerns about the risk of complications such as exposure of the mesh or the occurrence of *de novo* dyspareunia.[8–11] Despite the lack of proper scientific evidence, this new transobturator mesh technique was rapidly adopted in many countries. In the Cochrane 2010 database review on this subject, the need for adequately powered randomised trials was still emphasised.[12]

The objective of our trial was to test the hypothesis that the 12-month anatomical and functional results of a trocar-guided transobturator mesh procedure in primary surgical cystocele repair are superior to an anterior colporrhaphy.

Methods

Participants

Between June 2007 and May 2009, this study was conducted at one university medical centre and two large teaching hospitals in the Netherlands. Women aged 40–80 years, with bothersome pelvic organ prolapse complaints, a predominant cystocele ≥stage II (according to the Pelvic Organ Prolapse-Quantification [POPQ] system[13]) and an indication for surgical correction were eligible. Women of childbearing age were excluded if they had not completed their family or if they used inadequate birth control measures. Other exclusion criteria included: a history of urogynaecological surgery for pelvic organ prolapse or incontinence, concomitant urinary stress incontinence with an indication for surgical correction, a history of cancer or chronic obstructive pulmonary disease, recurrent lower urinary tract infections (more than three culture-proven infections/year), maximum bladder capacity <300 ml, and an indication for hysterectomy. To reflect daily practice as closely as possible, women needing additional surgical repair of a middle or posterior compartment pelvic organ prolapse were also included. Ethical approval for this study was obtained and all women signed informed consent. The study was internationally registered in the Netherlands Trial register under trial number NTR1376 (www.trialregister.nl).

Procedures

We set out to perform a randomised, assessor blinded, controlled trial. The mesh procedure included four skin incisions in the groin region that are not part of the anterior colporrhaphy. Assessor blinding for the allocated treatment was planned by bandaging of the groin before the physical examination at follow up. The woman was informed about the study by her gynaecologist, and after a minimal period of 1 week, she was contacted by a research nurse with information if she agreed to participate. For each centre, allocation was performed 1:1 by means of a computerised randomisation table that was available online on the study website. For all participants the selected procedure was checked with the actual surgical intervention data. The randomisation was stratified for the need to perform a sacrospinous hysteropexy in the case of a concomitant uterine prolapse or vaginal vault prolapse POPQ stage II or higher. As the mesh procedure includes four skin incisions, proper concealment of treatment could only be possible if these skin incisions were also performed in the anterior colporrhaphy group. This was considered to be non-ethical by both the investigators and the ethics committee.

Interventions

Six experienced gynaecologists, each having performed more than 20 trocar-guided transobturator mesh procedures before the start of the study, performed all of the procedures. To ensure standardisation of the mesh technique all surgeons were initially trained by the principal investigator (CHV). Formal re-evaluation of this standardisation was not performed during the study. Although the participating surgeons agreed on the anterior colporrhaphy technique, individual variations in skills may have existed. In the anterior colporrhaphy group, a midline incision of the vaginal epithelium was performed, and the bladder was sharply dissected from the vaginal wall. In contrast to the mesh procedure, no full thickness bladder dissection was performed. The pubocervical fascia was plicated in the midline with absorbable Vicryl® 2-0 interrupted sutures (Ethicon Inc, Somerville, NJ, USA). The surplus of vaginal epithelium was removed, and the epithelium was closed with running absorbable interlocking Vicryl 2-0. For the trocar-guided transobturator mesh repair of the cystocele, we used the Avaulta® anterior system (Bard, Covington, LA, USA). At the start of surgery, hydrodissection of the anterior vaginal wall with 20–30 ml of saline/epinephrine (1:200 000 dilution) was performed. After midline incision of the vaginal epithelium, a full thickness dissection of the bladder from the vagina was performed. The dissection was carried forward into the paravesical space up to the ischial spine and tendinous arc of the levator ani muscle. The mesh was placed with the use of four needle passages (outside–in, through the obturator foramen), according to the procedural guidelines of the mesh product. The anterior colporrhaphy and the mesh procedure were combined with a sacrospinous hysteropexy or a posterior colporrhaphy when indicated by judgement of the clinician. The sacrospinous hysteropexy was performed according to the technique described by Dietz et al.[14] All women received prophylactic antibiotics according to the local protocol and thrombosis prophylaxis. Postmenopausal women in the mesh group were all advised to use topical estrogens twice a week postoperatively. Although no scientific evidence exists, we believe that local estrogens may diminish the chance of mesh exposure.

Outcome measures

The following data were collected: age; date of surgery; obstetric history; surgical history; cardiovascular, pulmonary, endocrine and neuropsychiatric co-morbidity; drug use; perioperative and postoperative complications; stage of prolapse (POPQ), women requiring additional procedures; and symptom and quality of life scores. Exposure was defined when the mesh was seen or palpated in the incision line in the vagina. Erosion was defined as the appearance of mesh through the vaginal mucosa outside the incision line or into an adjacent organ.[15] Urinary retention was defined as >150 ml urine retention. Data were collected at baseline and at 6 and 12 months follow up. The primary outcome of our study was the difference in anatomical cure between the two interventions at 12 months follow up.

The stages of the pelvic organ prolapse, including the cystocele, were assessed in the lithotomy position using the POPQ system. Anatomical cure was defined as having a stage 0 or I cystocele at 12 months follow up. Women with a stage ≥II cystocele were considered failures. Assessment was performed by the surgeon or an independent gynaecologist. Assessor blinding for the allocated treatment during follow up was planned by bandaging of the groin before the examination. All assessors were trained and familiar with measurement of the POPQ system.

The secondary outcome of our study was the difference in symptom severity and quality of life at 12 months follow-up. A cystocele is not only associated with the classic bulging symptoms but can also be associated with bladder filling and emptying symptoms; as a consequence a symptom questionnaire that measures both was used. This questionnaire, the Urogenital Distress Inventory (UDI), has been validated for the Dutch population and consists of five domains: urinary incontinence, overactive bladder, pain, obstructive micturation and pelvic organ prolapse.[16,17] The scores of the UDI range between 0 and 100, with higher scores indicating increased symptom severity. Disease-specific quality of life was assessed with the Incontinence Impact Questionnaire (IIQ). The IIQ measures the impact of urogenital symptoms on quality of life in five domains: physical functioning, mobility, social functioning, embarrassment and emotional health. The score of the IIQ ranges between 0 and 100, with higher scores indicating a lower quality of life. In addition to the UDI and IIQ, two questions about dyspareunia were collected: 'Do you have sexual contact with your partner?' and 'Do you experience pain during sexual intercourse?'

The recurrence rate after an anterior colporrhaphy (POPQ ≥stage II) ranges between 20 and 70%.[4–6] At our institute, a 38% recurrence rate at 1 year has been reported.[7] Recurrence rates after synthetic mesh surgery in the anterior compartment ranges between 3 and 13%.[18,19] Our sample size calculation was based on this literature. We expected an anatomical failure rate at 1 year follow up of 35% in the anterior colporrhaphy group and 10% in the mesh group. To detect this difference, at a significance level of 0.05 and with a power of 0.80, 50 women had to be allocated to each group. With an estimated drop-out of 15%, a total of 115 women had to be randomised. During the inclusion period we decided to prolong the follow up to 5 years. With an estimated drop-out of 25% at 5 years, we had to increase the sample size to 125. The ethics committee approved this amendment to the protocol.

Data analyses

All analyses were performed according to the intention-to-treat principle. Data were collected in a web-based database and imported in the statistical SPSS-program (SPSS, version 16; SPSS Inc., Chicago, IL, USA). First, descriptive analyses of baseline characteristics of women in both groups were performed, using mean and standard deviations for parameters with a normal distribution and median and interquartile ranges for parameters with skewed distributions. Second, both baseline characteristics and outcome between treatment groups were compared using unpaired Student's *t*-test for normally distributed data, Mann–Whitney *U*-test for data with a skewed distribution, and Fisher's exact test for proportions. Analysis of the primary outcome included calculation of relative risks with confidence intervals, with the anterior colporrhaphy group as reference. Absolute risk reduction and numbers needed to treat were calculated when appropriate.

For the primary outcome, two extra scenarios were added to the analyses to assess the potential effect of missing POPQ stage data. First, the missing values at 12 months follow up were replaced with the last observation (6 months data) carried forward. Second, a worst-case scenario was used in which all women with missing POPQ scores at 12 months were scored as having a stage ≥II prolapse in all compartments.

Results

Participants

During the study period, 312 women were eligible and 125 were randomised. Figure 1 shows the flow of the participants through the trial. After randomisation and before surgery, four women withdrew from further participation. At 12 months, anatomical data were complete for 114 women, and functional data were complete for 110 women. Non-responders to the questionnaire were contacted by telephone. None of them reported having had a re-operation or hospital visit elsewhere. All reported having no new complaints. Baseline participant characteristics and prolapse staging are presented in Table 1. Except for the use of anti-depressive drugs in the mesh group ($P = 0.03$), no

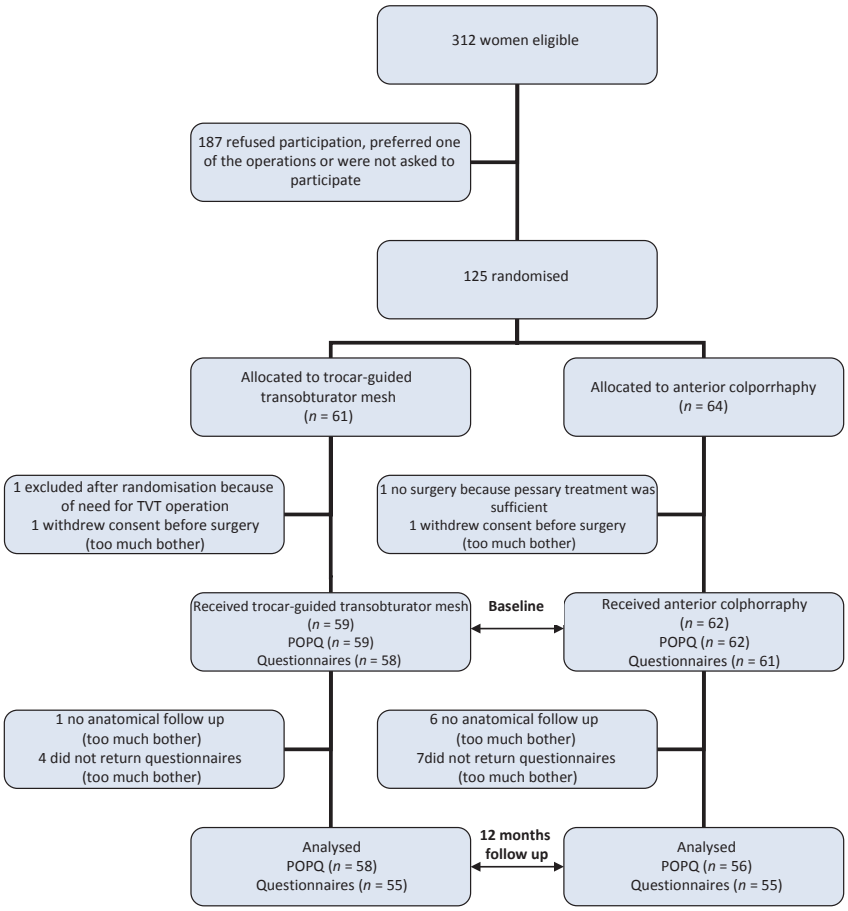

Figure 1. Flow of participants through the trial.

statistically significant differences in baseline characteristics were found (data on request). The distribution of POPQ stages between both groups was similar, with a majority of women having a stage III cystocele. During the study period all surgeons adhered to the protocol. Because of a reduction in financial support to the study, the use of independent research nurses for the planned assessor blinding procedure had to be interrupted during the conduction of the study. Instead, the majority of women were seen during follow up by their own gynaecologist who was aware of the procedure performed.

Anatomical outcome

In Table 2, the anatomical outcome after 12 months according to treatment group is shown. Compared with the anterior colporrhaphy group, the mesh procedure reduced the risk of anatomical failure (cystocele ≥stage II) at 12 months follow up from 59 to 9% (risk reduction 50.3%, 95% CI 35.5–65.1). The number needed to treat with the trocar-guided transobturator mesh to prevent one anatomical failure was 2 (95% CI, 1.5–2.8). However, only three women (5%) with anatomical failure in the anterior compartment after anterior colporrhaphy were scheduled for repeat surgery. Hence, the use of mesh resulted in an absolute risk reduction of needing repeat cystocele surgery of 5.4% (95% CI −0.5 to 11.3), with a corresponding number needed to treat of 19.

A *de novo* rectocele ≥stage II at 12 months follow up was diagnosed in ten women (23%) in the mesh group and five women (10%) in the anterior colporrhaphy group ($P = 0.16$). In the mesh group, two women with a *de novo* rectocele had surgery compared with one in the anterior colporrhaphy group. One woman in the colporrhaphy group received a pessary because of a stage II uterine prolapse.

In Table 2, the effects of the two scenarios, based on missing values (last observation carried forward and worst-case scenario), are shown. No statistically significant effect on the initial outcome was found.

Finally, we observed that approximately half of the study population needed a sacrospinous hysteropexy for middle compartment prolapse. This might have influenced

Table 1. Demographic and clinical characteristics according to surgical treatment groups

Characteristic	Trocar-guided transobturator mesh (*n* = 59)	Anterior colporrhaphy (*n* = 62)
Age (years), mean (SD)	60 (±9.1)	59 (±8.6)
Parity (number), mean (SD)	2.4 (±0.9)	2.7 (±1.9)
Body mass index (kg/m^2), mean (SD)	24 (±2.9)	24 (±3.6)
Preoperative POPQ staging		
Cystocele		
<Stage II	0 (0)	0 (0)
Stage II	15 (25)	14 (23)
Stage III	44 (75)	48 (77)
Uterine/vaginal vault prolapse		
<Stage II	30 (51)	31 (50)
≥Stage II	29 (49)	31 (50)
Rectocele		
<Stage II	43 (73)	49 (79)
≥Stage II	16 (27)	14 (21)
Combined procedures		
Sacrospinous hysteropexy	27 (46)	34 (55)
Posterior colporrhaphy	4 (7)	3 (5)
Perineal correction	3 (4)	4 (7)

Values are numbers (percentages) unless otherwise stated.

anatomical outcome per treatment group. For each treatment group, we performed a separate analysis, comparing anatomical and functional outcome for women with or without a sacrospinous hysteropexy. No statistical differences were observed (data on request).

Functional outcome

In Table 3, the median domain scores of the UDI and IIQ are shown before and at 12 months after surgery according to treatment group. Both groups showed a statistically significant improvement on all UDI domains ($P > 0.001$), except for the urinary incontinence domain in the mesh group ($P = 0.37$). All IIQ domain scores were significantly improved 12 months after surgery ($P > 0.001$), except for the embarrassment domain in the anterior colporrhaphy group ($P = 0.11$).

Two individual questions of the UDI relate specifically to the feeling or actually seeing of a vaginal bulge. Feeling a vaginal bulge was reported by 9% of women in each group after 12 months. Actually seeing a vaginal bulge was reported by 11% in the mesh group compared with 7% in the colporrhaphy group (not significant).

Of the women who responded to the questions about sexual functioning, the majority in both groups were sexually active, 32 out of the 50 women (64%) in the mesh group and 31 out of 48 women (65%) in the anterior colporrhaphy group ($P = 1.00$). Twenty sexually active women in the mesh group (40%) and 21 women in the anterior colporrhaphy group (43%) had no dyspareunia before surgery. *De novo* dyspareunia at 12 months follow up occurred in 3/20 (15%) women in the mesh group and 2/21 (9%) women in the anterior colporrhaphy group ($P = 0.66$). In total, 15 (24%) women preoperatively suffered from dyspareunia. This complaint resolved significantly more frequent after anterior colporrhaphy: after 12 months, in one out of five women in the mesh group, dyspareunia disappeared compared with eight out of ten women in the colporrhaphy group ($P = 0.018$).

Operative results and complications

Comparative surgical and perioperative data for both treatment groups are shown in Table 4. The majority of women received spinal anaesthesia (62%). Average operating time was 7 minutes longer for the mesh procedure ($P = 0.02$). One woman in the anterior colporrhaphy group and two women in the mesh group had tension-free vaginal tape procedures for stress incontinence performed during the follow-up period.

Within 12 months of surgery, two women had an exposure of the mesh. Both were successfully treated: one with local excision in the outpatient clinic and one surgically in the operating room. No erosions were observed. As shown in Table 4, overall re-operation rate was similar between both groups.

Discussion

Principal findings

In this multicentre randomised trial, we compared the anatomical and functional outcome of an anterior colporrhaphy with a trocar-guided transobturator mesh for primary cystocele repair. At 12 months follow up, anatomical cure was favoured by the trocar-guided transobturator mesh technique, showing an absolute risk reduction of 50.3% for recurrent cystocele stage II or III. However, the use of mesh showed an absolute risk reduction of only 5% in the need for surgery for a recurrent symptomatic cystocele. Both groups showed an equal significant functional improvement and preoperative and postoperative complications. Women with pre-existing dyspareunia were significantly more likely to have their dyspareunia resolved after an anterior colporrhaphy.

Explanation of results

Based on our primary outcome, e.g. anatomical cure, trocar-guided transobturator mesh surgery as primary repair for symptomatic cystocele stage ≥II, is to be recommended. However, most women with an anatomical failure lack symptoms, and likewise do not feel the need for a

Table 2. Twelve-month anatomical outcome according to surgical treatment group and different analysis strategies

Anatomical outcome	Trocar-guided transobturator mesh	Anterior colporrhaphy	
Primary analysis (complete follow-up)	**(*n* = 58)**	**(*n* = 56)**	**RR (95% CI)**
Cystocele			
<Stage II	53 (91%)	23 (41%)*	0.15 (0.06–0.35)
Stage II	5 (9%)	26 (46%)	
Stage III		7 (13%)	
Uterine/vaginal vault prolapse			
<Stage II	57 (98%)	54 (96%)	0.48 (0.05–5.18)
≥Stage II	1 (2%)	2 (4%)	
Rectocele			
<Stage II	42 (72%)	48 (86%)	1.93 (0.90–4.15)
≥Stage II	16 (28%)	8 (14%)	
Last outcome carried forward	**(*n* = 59)**	**(*n* = 62)**	
Cystocele			
<Stage II	54 (92%)	28 (45%)*	0.16 (0.07–0.37)
≥Stage II	5 (8%)	34 (55%)	
Uterine/vaginal vault prolapse			
<Stage II	58 (98%)	60 (97%)	0.53 (0.05–5.64)
≥Stage II	1 (2%)	2 (3%)	
Rectocele			
<Stage II	43 (73%)	52 (84%)	1.68 (0.83–3.40)
≥Stage II	16 (27%)	10 (16%)	
Worst-case scenario	**(*n* = 59)**	**(*n* = 62)**	
Cystocele			
<Stage II	53 (90%)	23 (37%)*	0.16 (0.07–0.35)
≥Stage II	6 (10%)	39 (63%)	
Uterine/vaginal vault prolapse			
<Stage II	57 (97%)	54 (87%)	0.26 (0.06–1.19)
≥Stage II	2 (3%)	8 (13%)	
Rectocele			
<Stage II	42 (71%)	48 (77%)	1.28 (0.69–2.35)
≥Stage II	17 (29%)	14 (23%)	

Values are numbers and relative risks (95% confidence Intervals) with the anterior colporrhaphy as reference group.
*P-value < 0.001.

surgical correction of what gynaecologists consider failure of treatment (i.e. anatomical recurrence). Recently, in a National Institutes of Health public access paper, Barber and co-workers[20] evaluated different definitions of surgical success in relation to the trial participants' own assessment of improvement and rating of success. They concluded that: 'the absence of vaginal bulge symptoms postoperatively has a significant relationship with a patient's assessment of overall improvement, while anatomic success alone does not.' Based on their results, they recommend adding the absence of bulge symptoms and absence of re-treatment to anatomical criteria to define success. When applying these criteria to our data, the number needed to treat with trocar-guided transobturator mesh to prevent one failure (re-operation) is 19. In addition, the focus in surgical intervention studies shifts towards a functional outcome instead of an anatomical outcome.[20,21] When applying this principal to our data there is no support for the use of mesh in primary cystocele repair.

In our study, the exposure rate of mesh after surgery was low (4%) compared with the 5–20% reported in other studies.[22–28] This may be explained by the fact that we did not combine the use of mesh with a hysterectomy,[28] and/or the collagen coating on the Avaulta® mesh, which might protect against exposure or erosion although the mechanism of action of this protection is unknown and hypothetical.[29]

Comparison with other studies

The high anatomical cure rate of synthetic mesh use in cystocele surgery in our series is comparable to that in the literature.[30] Most of the studies are prospective follow-up studies,[31–34] with only a limited number of randomised controlled trials comparing the use of anterior polypropylene mesh with anterior colporrhaphy.[22–24,27]

Table 3. Domain scores of the UDI and IIQ before and after surgery according to surgical treatment group

	Before surgery		12 months after surgery	
	Trocar-guided transobturator mesh (*n* = 58)	Anterior colporrhaphy (*n* = 61)	Trocar-guided transobturator mesh (*n* = 55)	Anterior colporrhaphy (*n* = 55)
UDI domains				
Genital prolapse	67 (33–67)	67 (33–67)	0 (0–0)	0 (0–0)
Overactive bladder	22 (11–44)	22 (0–44)	0 (0–11)	0 (0–22)
Urinary Incontinence	17 (0–33)*	17 (0–33)	17 (0–33)*	0 (0–17)
Obstructive micturation	17 (0–33)	17 (0–33)	0 (0–0)	0 (0–0)
Discomfort/pain	33 (0–50)	17 (0–50)	0 (0–17)	0 (0–17)
IIQ domains				
Emotional functioning	11 (0–33)	11 (0–22)	0 (0–11)	0 (0–11)
Physical functioning	17 (0–33)	8 (0–33)	0 (0–4)	0 (0–0)
Mobility	22 (11–33)	22 (0–33)	11 (0–22)	0 (0–11)
Social functioning	11 (0–22)	11 (0–22)	0 (0–0)	0 (0–6)
Embarrassment	0 (0–17)	0 (0–17)*	0 (0–0)	0 (0–0)*

P-value for difference between groups using Mann–Whitney *U*-test. Data presented as median (p25–p75).
All differences between baseline and 12-month data were statistically significant (*t*-test) at $P < 0.05$ except for those marked with an *.

These randomised controlled trials differ from our study with respect to the use of interpositioning of the mesh instead of our transobturator fixation,[23,24,27] the use of a mixed population of women with both primary and repeated cystocele repair instead of only primary cases,[22,27] the use of non-validated symptom and quality of life questionnaires,[27] and the use of a mixed population of cystocele and rectocele repairs.[24] Sivaslioglu et al.[23] studied primary repair but used a self-tailored mesh. In addition, women with a posterior compartment prolapse were excluded from their study. We decided not to exclude women with a combined pelvic organ prolapse because this reflects our daily practise. Carey and co-workers included only women with a combined cystocele and rectocele and used a mesh in both compartments.[24] Nguyen and Burchette[22] reported on the use of a transobturator mesh, but it was not stated whether all surgical procedures were primary repairs. The authors found similar anatomical and functional results as we did at 1 year follow up.

With a shifting definition of successful pelvic organ prolapse surgery towards a more patient-centred functional goal, complications like exposure and dyspareunia related to new techniques become increasingly important. The *de novo* dyspareunia rate in our study was slightly higher in the mesh group: 15% versus 9%. These results are comparable with other studies. Carey et al.[24] reported *de novo* dyspareunia in 16.7% in the mesh group and 15.2% in the no mesh group. The rates of *de novo* dyspareunia in the study by Nguyen and Burchette[22] were 9% in the mesh group and 16% in the no mesh group. This finding is the opposite of ours, but was also non-significant. Although the issue of *de novo* dyspareunia related to mesh surgery has raised concern, data from randomised controlled trials do not support this. *De novo* dyspareunia seems to be related to pelvic organ prolapse surgery in general,[35] not limited to the use of mesh, and is dependent on many additional factors.[36]

The significant higher cure rate of dyspareunia in the colporrhaphy group compared with the mesh group is an interesting finding, especially because postmenopausal women in the mesh group were advised to use topical estrogens and women in the anterior colporrhaphy group were not. However, these results should be interpreted with caution because of the low number of women involved.

Another issue associated with the use of transobturator mesh for cystocele repair is the risk of the occurrence of a *de novo* symptomatic rectocele. A recent observational study[37] showed a high rate of *de novo* prolapse (46%) in the unaffected compartment, especially after anterior mesh repair. Although we recorded a trend towards a higher risk of rectocele stage II or higher in the mesh group (22% versus 11%), this difference was non-significant.

Strengths and weaknesses

The major strength of our study is the multicentre, randomised trial design, which enhances the generalisability of our findings. Second, in daily practice, cystoceles are often accompanied by a prolapse of the apical or posterior vaginal compartment. By including these women in our study, we tried to reflect daily practice as much as possible.

Table 4. Surgical procedures and complications

	Trocar-guided transobturator mesh (*n* = 59)	Anterior colporrhaphy (*n* = 62)
Anaesthesia		
Total	23 (39%)	23 (37%)
Locoregional	36 (61%)	39 (63%)
Surgery time, minute (range)	48 (25–90)*	41 (20–80)*
Estimated blood loss, ml (range)	77 (5–400)	69 (5–800)
Duration of admission (days)	3 (±1.1)	3 (±1.1)
Duration of catheter (days)	2 (±1.2)	2 (±0.9)
Urinary retention (cc)	89 (±93)	81 (±121)
Postoperative complications during admission		
Retention bladder	12 (20%)	7 (12%)
Buttock haematoma	1 (2%)	0 (0%)
12 months	**(*n* = 58)**	**(*n* = 56)**
Mesh exposure	2 (4%)	–
Re-operation	6 (11%)	4 (7%)
Tension-free vaginal tape	2 (4%)	1 (2%)
Anterior mesh	0	3 (5%)
Posterior mesh	2 (4%)	0
Posterior colporhaphy	0	1 (2%)
Laparoscopic colpopexy	1 (2%)	0
Mesh exposure	1 (2%)	–
De novo dyspareunia	3/20 (15%)	2/21 (9%)
Cure of dyspareunia	1/5 (20%)*	8/10 (80%)*

Values are means (SD) or numbers (percentages).
All *P*-values calculated with independent *t*-test or Fisher exact test.
*$P < 0.05$.

By stratification and randomisation for repair of an apical prolapse, we ensured an equal distribution of the sacrospinous hysteropexy in both groups. We focused on women without prior prolapse surgery. Most other studies focus on the use of synthetic mesh in case of surgery for a recurrent cystocele. If a transobturator mesh as a primary procedure proves to be superior to an anterior colporrhaphy, the reduction in numbers of repeat surgery is beneficial from a woman's perspective as well as from an economic standpoint. Finally, we used validated internationally recognised outcome measures; this makes our study reproducible in other populations.[16,17] The major weakness of our study is the absence of assessment blinding at follow up. Approximately 60% of women were seen during follow-up visits by the specialist who also performed surgery. This may have introduced observation bias of the anatomical outcome, but not the functional outcome. The latter was assessed with self-administered questionnaires that were entered into the database by a research nurse. Another limitation is our follow-up time. Although 1-year follow up is common when reporting on outcome in these kinds of study, it is too short to draw definite conclusions on the recurrence and re-operation rate. A recent study showed that the majority of the recurrences occurred within the first year after surgery, which might indicate that a 1-year follow up would be sufficient.[24] Nevertheless, a 5-year follow up of our population has been planned. Finally, selection bias might have existed. Women who refused to participate in the study were offered an anterior colporrhaphy. Therefore, women could have chosen to participate in the study because they wanted to have the chance of getting mesh as primary treatment.

Conclusion

From a woman's perspective, the use of trocar-guided transobturator mesh in primary cystocele repair does not result in better functional outcome or a significant reduction in repeat surgery for symptomatic cystocele recurrence. Based on this perspective, the superior anatomical outcome at 1-year follow up does not justify its use in primary cystocele repair. Only long-term follow up will show if anatomical superiority persists and translates itself into fewer recurrences needing repeat surgery and better functional outcome. On the other hand, possible long-term complications of mesh, like erosion or dyspareunia, may limit its use.

Disclosure of interests

All authors have completed the Unified Competing Interest form at www.icmj.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) none of the authors have support from a company for the submitted work; (2) DG and CHV have financial relationships (honoraria and/or travel/accommodations payment for being an instructor at workshops) with Bard, Benelux V; none of the other authors have financial relationships that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) no non-financial interests that may be relevant to the submitted work.

Contribution to authorship

AV and CHV designed the trial protocol. AV and CHV coordinated the study. AV coordinated logistics and data collection. AV, KF and CHV analysed the data. All authors actively participated in interpreting the results and revising the papers. All authors approved the final manuscript.

Details of ethics approval

The University Medical Centre Utrecht Human Research Ethics Committee approved the study (project # 06/264), and all participants signed informed consent before taking

part. The trial is registered on www.trialregister.nl, registration number NTR 1376.

Funding
None.

Full trial protocol
Available on request from the corresponding author: avol lebregt@spaarneziekenhuis.nl.

Acknowledgements
None.

Supporting information

The following supplementary materials are available for this article:

Data S1. Powerpoint slides summarising the study.

Additional Supporting Information may be found in the online version of this article.

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Discussion points

1. Background: Debate how the woman's perspective compares with the surgeon's perspective for pelvic floor surgery.[1]
2. Methods: Describe the procedure in this study, in terms of intraoperative technique and postoperative follow up, and discuss how it compares with your practice. Was there a Standard Operating Procedure?

   Discuss the timing of randomisation and recruitment and how it might impact on drop-out rates of surgical intervention trials. Critically appraise the length of follow up in this study. Compare the outcome measures used in this study with those included in the Cochrane Systematic Review.[2]
3. Results and implications: Evaluate the results of this trial in the light of the absence of blinding. Discuss the use of local estrogen for women who had the mesh repair and any possible impact on outcome(s). With reference to the woman's perspective, discuss the outcomes for the index and control intervention in this study. Would you like to have additional information before changing your counselling for women who decide on cystocele repair? (Data S1). ■

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